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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,746	04/03/2001	Hans J. Hansen	018733-1015	1224

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N.	Applicant(s)
823,746	HANSEN et al
Examiner	**Group Art Unit**
SAUNDERS.	1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 11/27/02.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-65 is/are pending in the application.

Of the above claim(s) 53-56 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-52, 57-65 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

The claims pending are 1-65.

Applicant's election with traverse of Group I (claims 1-47) in Paper No. 5 (filed 11/27/02) is acknowledged. The traversal is on the ground(s) that the searches for the extra groups would not require an undue burden. This is not found persuasive because the restriction of Groups III and IV is proper for reasons set forth in Paper 4. However, upon reconsideration, the examiner concurs the search for Group II would not constitute an added search burden.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of a species (a), as the targetable conjugate is acknowledged.

Claims 1-52 and 57-65 of Groups I and II all read on the elected species and are under examination.

The disclosure is objected to because of the following informalities: at page 1, the related application data fails to refer to the provisional applications, for which applicant has claimed benefit in the declaration.

The current status of each of the variously recited copending applications (e.g. page 24) must be updated.

Appropriate correction is required.

Claim 17 is objected to because of the following informalities: In claim 17, line 2, the first recited isotope is incorrectly recited. It is believed that --18--, instead of "118", is intended as the superscript. Appropriate correction is required.

Applicant is advised that should claim 5 be found allowable, claim 12 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant is advised that should claim 4 be found allowable, claim 15 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant is advised that should claim 8 be found allowable, claim 17 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant is advised that should claims 6-7 be found allowable, claims 28-29 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 33-36 and 40-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims recite numerous, specific monoclonal antibodies. It is not clear that each of these publically available.

Applicant may address by showing that, for each specific antibody, any one of the following is applicable:

1) The monoclonal antibody is recited in a claim of an issued U.S. Patent, in which case it is presumed that the antibody is publically available.

2) The monoclonal antibody was commercially available from a public vendor (e.g. offered for sale in a catalogue or at a web site).

3) The complete V-region sequence of both H and L chains was known.

4) The hybridoma/cell line secreting the antibody has been deposited in accord with 37 CFR 1.801-1.809.

Claims 1-52 and 57-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing in the case in which the targetable conjugate "comprises an enzyme" because it is not clear which "enzymes", among the genus of enzymes, that part (D) applies to. Note that claim 12 recites "ribonuclease" and "DNAase I", which fall within the genus of

enzymes. However, claim 12 recites these as among the Genus of "toxins". Is the limitation of claim 1, part D) considered to be applicable to "ribonuclease" and "DNAase I" of claim 12 or not?

Claim 6 is unclear in reciting "further comprising a therapeutic nuclide" because it is not clear which component of claim 1 that the nuclide is attached to or intended to bind to. It is not clear as to which step of claim 1 that one is to administer the nuclide. It is believed that applicant intends to recite that the targetable conjugate comprises a therapeutic nuclide.

Claims 34 and 41 are unclear in relation to base claims 33 and 40, respectively. Each of the base claims requires the bispecific antibody to be comprised of two Fv components. Given this requirement it is not clear how these can become "chimerized" as recited in claims 34 and 41. Note the definition of a "chimeric antibody" as stated by applicant at page 30. Since Fv components have only variable, and no constant domains, it is not seen how one could consider an Fv, which has only a variable domain, as being "chimerized".

Claims 36 and 37 are unclear in relation to base claim 33. In like manner claims 43 and 44 are unclear in relation to base claim 40. Each of the base claims requires the bispecific antibody to be comprised of two Fv components. Each Fv would necessarily contain all six CDRs of the Fv domain. It is thus not seen how one can recite in claims 36-37 and 43-44 that the bispecific antibody could comprise only "one or more of the CDRs...".

In claims 48, 52, 55 and 61-63 it is not clear which moiety of the targetable conjugate that the "other arm" of the bispecific antibody binds to. Is it to the HSG?

In claims 48, 52, 55 and 61-62 Markush group members (d) and (e) are indefinite. It is not clear what the squiggly bond between the "NH" and "D-Ala" represents.

In claim 59, line 1 "said virus" lacks antecedent basis.

In claim 60, line 1 "said bacterium" lacks antecedent basis.

Claims 61, 62 and 63 are unclear by reciting "intraoperatively", "endoscopic" and "intravascular" respectively. After "comprising" each of these claims recites precisely the same steps (which are also precisely the same steps recited in claim 57). There is no step referring to an operation, to an endoscope or to an I.V. injection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-9, 11-13, 16-17, 19-22, 24-25 and 28-31 are rejected under 35 U.S.C. 102(b) as being entirely anticipated by Barbet et al. (5,274,076).

Barbet et al. ('076) disclose a "probe" component (product (b)) which contains (HSG) moieties. See particularly col. 3, lines 18-19; the last structure spanning cols. 3-4; Example 3; and claims 3 and 5. These are designed to be conjugated to an

imaging or therapeutic moiety -- e.g. a chelator for a radioisotope, paramagnetic ions, toxins, cytotoxic drugs, porphyrins. Barbet et al. ('076) teach use of such probe products in conjunction with a bispecific antibody and in a manner consistent with instant claim 1, parts (A) and (C). See col. 1, lines 15-49 and col. 5, lines 24-55. In this rejection Barbet et al.'s "probe" product corresponds to the instant "targetable conjugate".

With respect to instant claim 2, Barbet et al. do not ipsi verbis recite the range of KeV; however, among the numerous isotopes recited at col. 4, lines 15-63, are numerous examples of those which applicant has disclosed (page 20) as providing radiant energy within the recited range. Thus claim 2 is inherently anticipated.

Concerning instant claims 3, 5 and 11-12 note toxins taught at col. 2, lines 60-61 and col. 5, lines 20-23.

Regarding claims 6-9, 16-17 and 28-29 note teachings at col. 4, lines 15-63.

With respect to claim 13, the various chemotherapeutic agents at col. 2, lines 57-61 and col. 5, lines 17-20 are properly considered as "drugs".

For claims 16 and 31, note that Barbet et al. teach targeting to a "pathological component" (col. 5, lines 34, 43) or a tumor (col. 5, line 53).

Concerning claims 16 and 19-20, note the teachings of Gd, Fe and Mn as paragmagenetic labels, which would have been immediately recognized by one of skill as detectable by MRI.

Regarding claims 21-22, note teachings of the photosentization of porphyrins at col. 2, lines 61-62. The porphyrin is inherently a "photosensitizer."

With respect to claims 24-25, note teachings of monoclonal antibodies and their fragments at col. 1, line 19-29 and col. 5, lines 27-40.

Concerning claim 30, note teaching of "methotrexate" at col. 2, line 61 and col. 5, line 18.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-31 and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet ('076) in view of Hansen et al. (WO 99/66951).

It is firstly to be noted that citation of Hansen et al. is proper because it predates the instant filing date by more than one year. The instant claims are only granted benefit of the instant CIP application filing date, because the parent recites nothing about a histamine-succinyl-glycine (HSG) hapten.

Barbet have been noted supra, under 102(b), as anticipating claim 1 and numerous dependent claims. Hansen et al. teach all aspects of the instant invention but for the use of HSG as the hapten. However given the teachings of Barbet et al. it would have been obvious that the bispecific antibodies and the HSG containing probes (corresponding to the instant targetable conjugate), would be useable in any of the targeting methods taught by Hansen et al.

The teachings of Hansen et al. with respect to numerous of the imaging or therapeutic agents recited in the dependent claims that have been rejected over Barbet et al. are cumulative. As to the features of instant claims not taught by Barbet et al., Hansen et al. are relied upon for the following teachings.

Hansen et al. teach use of clearing agents and teach use of enzymes in the targetable conjugate -- e.g. see claim 1 at page 58. They thus teach parts (B) and (D) of instant claim 1.

With respect to claims 3-4, 14-15 and 30 note teachings of "prodrugs" and species thereof by Hansen et al. at page 29.

With respect to instant claim 10, note claim 4 of Hansen et al.

Regarding instant claim 18, see claim 11 of Hansen et al.

For instant claims 21-23, note page 27 of Hansen et al.

Concerning instant claims 26-27, see claims 14-15 of Hansen et al.

Regarding the fusion protein of instant claim 38, see page 19 of Hansen et al.

Regarding the CEA of instant claim 39 see pages 10, 17 and 20 of Hansen et al. For example.

Claims 1 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet et al. ('076) in view of Primus et al. (4,818,709).

Barbet et al. have been cited supra against claim 1. Primus et al. teach (col. 19, line 52) that CSAp is a desirable target antigen for in vivo immunoimaging or immunotherapy. Thus

it would have been obvious to use bispecific antibodies targeted against CSAb in the method of Barbet et al.

Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet et al. ('076) in view of Hansen et al. (WO 99/66951) as applied to claims 1 and 39 above, and further in view of Primus et al. ('709).

Barbet et al. and Hansen et al. have been noted supra for teaching immunoimaging or immunotherapy methods using bispecific antibodies targeted to CEA. Primus et al. teach the further feature that antibodies directed to CEA Class III epitopes are specific for CEA and avoid cross reactions with MA and NCA. They teach that antibodies specific for CEA are desirable for use in vivo immunoimaging or immunotherapy (e.g. col. 2, lines 3-12). Thus it would have been obvious to employ bispecific antibodies targeted to a CEA Class III epitope in the method of Barbet et al.

Claims 1 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet et al. ('076) in view of Goldenberg (6,096,289).

Barbet et al's. teachings have been discussed supra for claim 1. Like Barbert et al's., Goldenberg teaches the use of bispecific antibodies for in vivo localization and/or therapy of

a targeted tissue/cell type. Goldenberg teaches that CSAp is an appropriate antigen to be targeted in the treatment or imaging of tumors (e.g. col. 18, line 8). Therefore it would have been obvious to use bispecific antibodies that target CSAp in conjunction with the imaging/therapeutic agents conjugated to two HSG haptens taught by Barbet et al.

Claims 33-37, 40-46, 48-52 and 57-62 contain limitations allowable over the prior art of record which does not teach Mab 679 and does not teach the conjugates recited in claims 48, 52, 57 and 61-62.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan , can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

March 03, 2003

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644